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(54) PROCESS FOR THE PREPARATION OF TETRAFLUOROETHYL PHENYL ETHERS

(71) We, FARBWERKE HOECHST AKTIENGESELLSCHAFT, vormals Meister Lucius & Brüning, a Body Corporate recognised under German Law, of 6230 5 Frankfurt (M)-Hoechst, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following 10 statement:—

The present invention relates to an improved process for the preparation of $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl phenyl ethers from phenols or phenolates and tetrafluoroethylene.

15 It is already known that phenyl-tetrafluoroethyl ethers can be prepared by reacting phenols with tetrafluoroethylene in an anhydrous medium in the presence of catalytic amounts of sodium metal (cf. D. C. England 20 et al., Am. Soc. 82 (1960) p. 5116—5122). According to Sheppard, J. Org. Chem. 29 (1964), p. 1—11, it is possible to obtain *m*-nitrophenyltetrafluoroethyl ether by the reaction of tetrafluoroethylene with *m*-nitrophenol in the presence of catalytic amounts of 25 sodium hydride in anhydrous dimethoxyethane.

The two processes referred to above are 30 complicated and expensive because the reaction has to be carried out with complete exclusion of water, and when using sodium and sodium hydride this requires special steps. Moreover, the yields provided by these processes are only from 50 to 70%.

35 W. J. Pummer and L. A. Wall, SPE Transactions, Vol. 3 (1965), p. 220—224, have attempted to carry out this reaction in the presence of water using hydrated sodium phenolate and an excess amount of tetrafluoroethylene in dimethylformamide at a raised temperature and pressure. In this case, however, $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl-phenyl ether was obtained in a yield of only 23.5%, whereas the main products of this reaction were 45 high molecular-weight products, i.e. pre-

sumably polymeric perfluorovinyl phenyl ethers or addition products of 2 mols of phenol on 1 mol of tetrafluoroethylene.

The present invention is based on the observation that $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl phenyl ethers can be obtained in a simple and advantageous manner from phenols and tetrafluoroethylene at a raised temperature and under pressure in a solvent which is miscible with water and does not react with tetrafluoroethylene, by reacting the phenols and alkali metal hydroxides or alkali metal salts of the phenols in the presence of water with tetrafluoroethylene, while preferably maintaining a molar ratio of tetrafluoroethylene to phenol or phenolate used in the range of from 1:20 to 1:1 during the reaction.

As alkali metal hydroxides, potassium hydroxide or sodium hydroxide are preferred, which may also be used in an aqueous solution. When solid alkali metal hydroxide is used, the water formed by the equilibrium reaction between phenol and alkali metal hydroxide provides the necessary water for the reaction of the invention. An advantageous modification of the process is the use of aqueous potassium or sodium salts of the phenols.

The reaction is carried out at temperatures within the range of from 40 to 150°C, preferably from 60 to 100°C, under pressures of from 2 to 40 atmospheres gauge, preferably from 4 to 10 atmospheres gauge. The alkali metal hydroxide which functions as catalyst is used in amounts within the range of from 0.05 to 0.5 mol, preferably from 0.1 to 0.4 mol, per mol of phenol. The minimum content of water required for the reaction of the invention is determined by the amount of catalyst. It is preferable to use within the range of from 0.1 to 3 mols of water per mol of phenol or phenolate. The use of larger amounts of water is possible, but will generally not give any advantage.

As solvents which are miscible with water

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[Price 25p]

and do not react with tetrafluoroethylene, there are used, in addition to dimethylformamide or dimethoxy-ethane already disclosed for this purpose, acetone, dimethylsulphoxide, tetrahydrofuran or dioxane.

As starting materials there are mentioned, in addition to unsubstituted phenol or phenolate, mono-, di- and tri-substituted phenols or phenolates. The phenol radical may then be substituted, by for example, an alkyl group having up to 20, preferably up to 4 carbon atoms, an alkoxy group having up to 20, preferably up to 4 carbon atoms, a nitro group, an amino group, an alkylamino group having up to 20, preferably up to 4 carbon atoms or a dialkylamino group, the alkyl radicals of which contain up to 20, preferably up to 4 carbon atoms. In the case of dialkyl-amino groups, the two alkyl groups together with the nitrogen atom may form a saturated heterocyclic ring. Thus, for example, *o*-, *m*-, *p*-nitrophenols, aminophenols, dimethyl-aminophenols, anisol, phenetol and butoxy-phenols are used as starting materials.

It is critical, for the reaction of the invention, that the molar ratio of tetrafluoroethylene to phenol or phenolate should not at any time during the reaction exceed 1. A suitable way of carrying out the reaction is to add the tetrafluoroethylene in a number of small portions. It is, therefore, advantageous to react the tetrafluoroethylene gradually in the gaseous state. It is preferable, in the process of the invention, that the components be reacted continuously.

The reaction carried out according to the invention is advantageous in comparison with the known processes because the reaction rate and yields are substantially higher. For example, the yields obtained by the present process all exceed 80%. The reaction rate is especially higher when substituted phenols are used: the reaction of *m*-nitrophenol by the process of the invention is completed after only two hours, whereas the reaction according to the known processes using sodium metal as a catalyst provides yields of from only about 5 to 10% after two hours.

A further advantage is that a harmless and moisture-insensitive catalyst is employed which enables non-absolute industrial solvents to be used. The fact that alkali metal hydroxide can be used in the form of an aqueous solution offers particular advantages of dosing, above all when the process is carried out continuously. It is furthermore advantageous that phenols or phenolates which, in many cases, are stored as solids (containing about 25% water) for reasons of safety, especially nitrophenols and derivatives thereof, can be used directly without further purification.

The products of the invention are intermediates suitable for use in a variety of in-

dustrial fields, mainly for the synthesis of dyes or plant-protective agents.

The following examples illustrate the invention, the parts and percentages being by weight unless otherwise stated.

EXAMPLE 1

In an autoclave, 700 ml of dimethylformamide and 20 g (0.35 mol) of potassium hydroxide were added to 307 g (2.21 mols) of *m*-nitrophenol and the mixture heated to 80-90°C after flushing with nitrogen. Subsequently, tetrafluoroethylene was pressurized to a pressure of 8 atmospheres gauge, and maintained at this pressure until a slow-down of the drop in pressure indicated the end of the reaction. The pressure was then allowed to drop to a large extent. After cooling, the majority of the solvent was distilled off and the residue washed with water, dried and distilled.

Yield: 440 g (=83%) of *m*-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.

Boiling point: 93°C under a pressure of 2 mm mercury, $n_D^{25}=1.4553$.

The isolated product had a purity of 99.3%.

EXAMPLE 2

306 g (2 Mols) of 2-methyl-4-nitrophenol were reacted with tetrafluoroethylene as described in Example 1.

437.1 g (=86.5%) of 2-methyl-4-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether were obtained.

Boiling point: 93°C under a pressure of 1 mm mercury, $n_D^{25}=1.4660$.

Analysis of nitrogen:

Calculated: N 5.52%.

Found: 5.6%.

The compound had a purity of 99.6%.

EXAMPLE 3

306 g (2 Mols) of 2-methyl-4-nitrophenol were dissolved in 700 ml of dimethylformamide, 40 g of a 50%-aqueous solution of NaOH were added thereto and the mixture was reacted with tetrafluoroethylene.

Yield: 435.5 g (=86%) of 2-methyl-4-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.

The physical data corresponded to the values mentioned in Example 2.

EXAMPLE 4

139 g (1 Mol) of *o*-nitrophenol were reacted with tetrafluoroethylene at 80-90°C in the presence of 14.4 g (0.36 mol) of NaOH as a catalyst, in the manner disclosed in Example 1.

Yield: 195.9 g (=82%) of *o*-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.

Boiling point: 70°C under a pressure of 0.3 mm mercury $n_D^{25}=1.4537$.

EXAMPLE 5

20 g of KOH were added to 139 g (1 mol)

of *o*-nitrophenol and the mixture was reacted with tetrafluoroethylene as described in Example 1.

5 Yield: 212.7 g (=88.5%) of *o*-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoro ethyl ether.
The physical data correspond to the values mentioned in Example 4.

EXAMPLE 6

10 139.11 g (0.7 Mol) of potassium *o*-nitrophenolate containing 13 g (10%) of water were reacted with tetrafluoroethylene as described in Example 1, except that no catalyst was added.

15 Yield: 198 g (=83%) of *o*-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.
The physical data corresponded to the values mentioned in Example 4.

EXAMPLE 7

20 161.1 g (1 Mol) of sodium *p*-nitrophenolate containing, in addition 53.7 g (25%) of water, were reacted with tetrafluoroethylene in the manner described in Example 1, except that no catalyst was added.

25 Yield: 200.2 g (=88.5%) of *p*-nitrophenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.

Melting point: 42–44°C.
Calculated: C 40.2 H 2.09 N 5.85 F 31.8.
Found: 39.8 2.1 6.2 30.8.

EXAMPLE 8

30 470.55 g (5 Mols) of phenol were reacted with tetrafluoroethylene in 500 ml of dimethylformamide, in the presence of 28.05 g (0.5 mol) of KOH as a catalyst, in the manner described in Example 1.

35 Yield: 807.8 g (=83%) of phenyl- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.
Boiling point: 88–91°C under a pressure of 90 mm mercury (compare England et al., J. Am. Chem. Soc. 82 (1960) p. 5117; 40 boiling point 147°C under a pressure of 760 mm mercury).

EXAMPLE 9

45 450 g (3 Mols) of *o*-sec.-butylphenol were reacted with tetrafluoroethylene in 700 ml of dimethylformamide in the presence of 20 g (0.358 mol) of KOH, as a catalyst, in the manner described in Example 1.

50 Yield: 610 g (=81.3%) of *o*-sec.-butylphenol- $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl ether.
Boiling point: 86°C under a pressure of 14 mm mercury. $n_D^{25}=1.4315$.
Calculated: C 57.6 H 5.65 F 30.4.
Found: 57.4 5.5 30.8.

EXAMPLE 10

55 In an autoclave having a capacity of 10 litres, 2180 g (20 mols) of 3-aminophenol were dissolved in 4 l of dimethylformamide and 200 g (3.57 mols) of KOH were added thereto. The reaction with tetrafluoroethylene 60 was carried out as described in Example 1.

The product was obtained in a pure form by distillation using a 120-cm packed column.

Yield: 3,400 g (81%) of 3-aminophenyl-tetrafluoroethyl ether, purity: 98%.

Boiling point: 112–114°C under a pressure of 15 mm mercury, $n_D^{20}=1.4608$.

For comparisons sake: W. A. Sheppard, J. Org. Chem. 29, p. 5 (1964): $n_D^{25}=1.4636$.

Boiling point: 100°C under a pressure of 6.6 mm mercury.

EXAMPLE 11

A mixture of

3,000 g (27.5 mols) of 3-aminophenol, 310 g (5.6 mols) of KOH and 4 litres of acetone

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was reacted with tetrafluoroethylene as described in Example 1 in an autoclave having a capacity of 10 litres. Distillation was carried out using a short column and 4650 g (81%) of 3-aminophenyl-tetrafluoroethyl ether were obtained. The properties corresponded to those indicated in Example 10.

EXAMPLE 12

In a storage tank, a mixture was prepared, while stirring, from the following components:

44.2 % of 3-aminophenol
48.7 % of dimethylformamide
4.55 % of KOH and
2.51 % of H₂O.

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First the 3-aminophenol was dissolved in dimethylformamide and then KOH in an aqueous solution was added in doses.

The mixture was subsequently pumped into a 2–1 autoclave heated to 80°C, until a filling of 1,000 cc was reached. While stirring, 8 atmospheres gauge of tetrafluoroethylene were pressurized and maintained until the pressure no longer dropped. 350–400 ml of the reaction mixture thus formed were withdrawn by means of an immersion pipe and replaced by fresh solution pumped in by means of the pump. This operation was continued until 12,535 kg of 3-aminophenol yielded 40.1 kg of a crude reaction mixture from which 21.95 kg of 3-aminophenyl-tetrafluoroethyl ether were obtained in a purity of 99.3%, by means of fractional distillation (using a 80 cm column packed with VA-steel wire rings). The boiling point was 122–125°C under a pressure of 22 mm mercury; 11.7 kg of tetrafluoroethylene had been consumed. The yield was

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91.5%, calculated on the 3-aminophenol and
90 %, calculated on the tetrafluoroethylene used and

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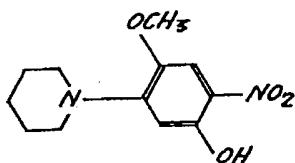
The conversion was almost quantitative.

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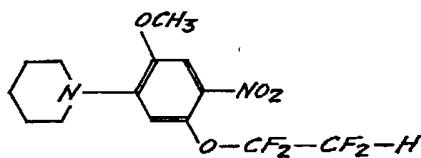
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EXAMPLE 13

80 g (0.318 Mol) of 2-nitro-4-methoxy-5-piperidino-phenol



5 and 3.15 g (0.057 mol) of KOH were reacted with tetrafluoroethylene in 250 ml of dimethylformamide as described in Example 1. Subsequently, the dimethylformamide was distilled off and the crystallized precipitate 10 was recrystallized from methanol. 92 g (82%) of pure (2 - nitro - 4 - methoxy - 5 - piperidino - phenyl) - tetrafluoroethyl ether of the formula



15 were obtained. Melting point 103—105°C. C₁₄H₁₄F₄N₂H₄ (molecular weight 352) Calculated: C 47.4 H 4.55 N 7.95 F 21.6. Found: 47.4 4.7 8.2 23.3.

WHAT WE CLAIM IS:—

20 1. A process for the preparation of $\alpha,\alpha,\beta,\beta$ -tetrafluoroethylphenyl ethers from phenols or phenolates and tetrafluoroethylene, which comprises reacting a phenol and an alkali metal hydroxide or an alkali metal phenolate with tetrafluoroethylene in a water-miscible solvent at a temperature within the range of from 40 to 150°C and at a pressure within the range of from 2 to 40 atmospheres gauge in the presence of water, the molar ratio of the tetrafluoroethylene used to the phenol or phenolate being not greater than 1.

25 2. A process as claimed in claim 1, wherein the molar ratio of the tetrafluoroethylene to the phenol or phenolate during the reaction is within the range of 1:20 to 1:1.

30 3. A process as claimed in claim 1 or 2, wherein the reaction is carried out at a temperature within the range of from 60 to 100°C.

35 4. A process as claimed in any one of claims 1 to 3, wherein the reaction is carried out at a pressure within the range of from 4 to 10 atmospheres gauge.

40 5. A process as claimed in any one of claims 1 to 4, wherein the amount of water present

is within the range of from 0.1 to 3 mols per mol of phenol or phenolate.

45 6. A process as claimed in any one of claims 1 to 5, wherein the tetrafluoroethylene is added portionwise.

7. A process as claimed in any one of claims 1 to 6, wherein gaseous tetrafluoroethylene is used.

8. A process as claimed in any one of claims 1 to 7, wherein the reaction is carried out continuously.

9. A process as claimed in any one of claims 1 to 8, wherein the phenol is substituted by one to three substituents.

10. A process as claimed in claim 9, wherein the phenyl radical is substituted by an alkyl group having up to 20 carbon atoms, an alkoxy group having up to 20 carbon atoms, a nitro, amino, alkylamino having up to 20 carbon atoms or dialkylamino group, the alkyl radicals of which contain up to 20 carbon atoms and can be connected to form together with the nitrogen atom a saturated heterocyclic ring.

11. A process as claimed in claim 10, wherein the phenol is substituted by an alkyl group having up to 4 carbon atoms, an alkoxy group having up to 4 carbon atoms, a nitro group, an amino group, an alkylamino group having up to 4 carbon atoms or a dialkylamino group, the alkyl radicals of which contain up to 4 carbon atoms and can be connected to form together with the nitrogen atom a saturated six-membered heterocyclic ring.

12. A process as claimed in claim 10, wherein the substituted phenol is o-, m- or p-nitrophenol, aminophenol, dimethyl-amino-phenol, anisol, phenetol or butoxy-phenol.

13. A process as claimed in any one of claims 1 to 12, wherein sodium hydroxide is used as catalyst.

14. A process as claimed in any one of claims 1 to 12, wherein potassium hydroxide is used as catalyst.

15. A process as claimed in any one of claims 1 to 14, wherein an aqueous solution of the alkali metal hydroxide is used.

16. A process as claimed in any one of claims 1 to 12, wherein an aqueous alkali metal phenolate is reacted with tetrafluoroethylene.

17. A process as claimed in any one of claims 1 to 15, wherein 0.05 to 0.5 mols of alkali metal hydroxide is used per mol of phenol.

18. A process as claimed in claim 17, wherein 0.1 to 0.4 mols of alkali metal hydroxide is used per mol of phenol.

19. A process as claimed in any one of claims 1 to 18, wherein the solvent which is miscible with water is dimethylformamide, dimethoxy-ethane, acetone, dimethylsulphoxide, tetrahydrofuran or dioxane.

20. A process according to claim 1 and conducted substantially as described in the Examples herein.

5 21. $\alpha,\alpha,\beta,\beta$ -tetrafluoroethyl-phenyl ethers whenever prepared by a process as claimed in claims 1 to 20.

ABEL & IMRAY,
Chartered Patent Agents,
Quality House,
Quality Court,
Chancery Lane,
London, W.C.2.

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